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10/659,423

09/10/2003

Tammy Burd Mehta

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05/10/2006

CALIPER LIFE SCIENCES, INC.

605 FAIRCHILD DRIVE

MOUNTAIN VIEW, CA 94043-2234

EXAMINER

BABIC, CHRISTOPHER M

ART UNIT

PAPER NUMBER

1637

DATE MAILED: 05/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |   |  |  |
|------------------------------|---|--|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/659,423    | <b>Applicant(s)</b><br>MEHTA, TAMMY BURD |  |
|                              | <b>Examiner</b><br>Christopher M. Babic | <b>Art Unit</b><br>1637                  |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 07 March 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-10 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of the Claims***

Claims 1 and 3-10 are pending. The following Office Action is in response to Applicant's response dated March 7, 2006.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

**1. Claims 1, 3-7, and 10 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Stapleton (U.S. 5,188,963) in view of Moreira ("Efficient removal of PCR inhibitors using agarose-embedded DNA preparations" Nucleic Acids Research. 1998. Vol. 26, No. 13: Pages 3309-3310).**

With regard to Claims 1 and 3, Stapleton discloses methods of samples to be analyzed for the presence of a particular DNA component comprising: (a) amplifying a desired nucleic acid component in matrix material; and (b) applying an electric current to the matrix material (Column 3, Lines 20-40, for example). Stapleton further discloses the matrix as being a semi-solid material made with agarose or acrylamide or similar

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polymer, or mixture thereof (Column 8, Lines 40-65). Stapleton further discloses that this research clearly demonstrates amplification in agarose gels by the Polymerase Chain Reaction (PCR) with Taq polymerase (Column 12, Lines 20-35, for example). Stapleton discloses several examples (Columns 14-18; especially Example 2) wherein PCR amplification followed by electrophoretic separation is performed within a "sieving matrix" Stapleton does not specifically disclose ranges of polymer concentration.

Moreira discloses that agarose-embedded DNA can be directly used for PCR since low melting point (LMP) agarose does not interfere with the reaction (Abstract). Moreira further discloses agarose-embedded DNA is useful for PCR, since reactions are not affected by the presence of high quality LMP agarose concentrations even as high as 0.3% in the PCR mixture (Page 3309, Column 2, End Paragraph 1).

Based on the combined disclosures of the applied references, one of ordinary skill in the art at the time of invention would have had a reasonable expectation of success practicing the methods set forth by Stapleton further comprising a polymer solution comprising less than about 0.4% polymer. The motivation to do so, provided by Moreira, would have been the discovery that PCR is unaffected by low polymer concentration. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the instant methods as claimed.

With regard to Claims 4 and 5, Stapleton discloses acrylamide or similar polymer, or mixture thereof (Column 8, Lines 40-65). It is noted that the Moreira reference discloses PCR in the presence of agarose only, however, Stapleton does disclose a polyacrylamide gel concentration of 5% (Column 15, Lines 5-10, for example). The

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demonstration of PCR in the presence of a polyacrylamide concentration of 5% would have given one of ordinary skill in the art a reasonable expectation of success practicing a PCR reaction in the presence of a *more fluidic* polyacrylamide concentration comprising less than about 0.4% polymer. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the instant methods as claimed.

With regard to Claim 6, Stapleton discloses the matrix as being a semi-solid material made with agarose (Column 8, Lines 40-65).

With regard to Claim 7, Stapleton discloses PCR with Taq polymerase (Column 12, Lines 20-35, for example).

With regard to Claim 10, Stapleton discloses electrophoretic separation (Columns 14 and 15, Example 2, for example).

**2. Claims 8 and 9 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Stapleton (U.S. 5,188,963) in view of Moreira ("Efficient removal of PCR inhibitors using agarose-embedded DNA preparations" Nucleic Acids Research. 1998. Vol. 26, No. 13: Pages 3309-3310), in further view of Woolley et al. "Ultra-high-speed DNA fragment separations using microfabricated capillary array electrophoresis chips" Proc. Natl. Acad. Sci. November 1994. Vol. 91: Pages 11348-11352).**

With regard to Claims 8 and 9, the methods of Stapleton and Moreira have been outlined in the above rejections. Neither Stapleton nor Moreira specifically disclose methods within microfluidic channels.

Woolley et al. disclose mixing a PCR reaction component with a sieving matrix and subsequent electrophoretic separation within a microfluidic channel (Page 11349, Column 2, Electrophoresis Procedures; Figure 2, for example).

Based on the combined disclosures of the applied references, one of ordinary skill in the art at the time of invention would have had a reasonable expectation of success practicing the methods set forth by Stapleton and Moreira within a microfluidic channel. At the time of invention, the disclosure of Woolley et al. clearly would have provided the instruction necessary for one of ordinary skill in the art to practice the methods as claimed. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the instant methods as claimed.

***Response to Arguments - Claim Rejections - 35 USC § 103***

Applicant's arguments with respect to the rejections in view of the applied references have been fully considered but they are not persuasive.

With specific regard to the Stapleton and Moreira references, Applicant argues that the combination of the cited references does not teach or suggest all of the claimed limitations of Claim 1. Applicant further argues that Moreira teaches away from performing both PCR and electrophoresis in a PCR sieving medium having "less than

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about 0.4% polymer" because Moreira teaches electrophoresis of PCR products on a 1.2% gel.

First, Applicant is correct in asserting that Moreira teaches agarose concentrations "even as high as 0.3%" are used in sample preparation to isolate large DNA's from cell debris and contaminants, resulting in a purified gDNA, however, that fact is irrelevant to the disclosure of PCR in agarose concentrations "even as high as 0.3%" (Page 3309, Column 2, End Paragraph 1). Moreira clearly teaches PCR within agarose concentrations "even as high as 0.3%". Furthermore, Applicant is correct in asserting that Moreira teaches electrophoresis of PCR products on a 1.2% gel, however, that particular method step is necessitated by the *size* of the PCR product. Moreira teaches the amplification and resolving of a 0.6 kb and 0.85 kb fragment, which require that agarose gel concentration. It was a well-known scientific fact at the time of invention that agarose gels having different polymer concentrations have different ranges of separation of linear DNA molecules. A larger amplification product (i.e. greater kb length) requires polymer mixture of less concentration for accurate separation. It would have been *prima facie* obvious to a practitioner of ordinary skill in the art at the time of invention to incorporate a lower agarose concentration to resolve an amplification products of larger size (i.e. greater kb length).

Thus, the rejections are maintained.

### **Conclusion**

**Claims 1 and 3-10 are rejected. No claims are allowed.**

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Maniatis et al. *Molecular cloning: a laboratory Manual*. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY (1982): pages 150-152.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.



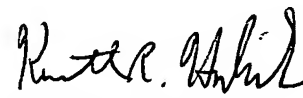
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

 5/2/06

Christopher M. Babic  
Patent Examiner  
AU 1637

  
KENNETH R. HORLICK, PH.D  
PRIMARY EXAMINER

5/8/06